Antimicrobial Studies of Some 1,1-Bis-[2-Hydroxy-3-(3-Aryl-Prop-2-en-1-one)-5-Methyl Phenyl] Methanes and Their Dibromo Derivatives

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Some bis-chalcones and their bromo derivatives were synthesized and tested for antimicrobial activities against *S. aureus, E. coli, Pr. mirabilis, Ps. aeruginosa, E. aerogenes, S. typhi and Pr. Vulgaris.* The titled compounds were found effective against amost all micro-organisms.

INTRODUCTION

The presence of enone function in the chalcone molecule confers the antibiotic activity[1–3]. This property is enhanced when substitution is made at α and β-positions[4]. Chalcones and their substituted derivatives[5,6] included in some heterocyclic analogues have been reported to possess some interesting biological properties with detrimental growth of microbes[7,8].

Literature survey shows that antimicrobial activities of 1,1-bis-[2-hydroxy-3-(3-aryl-prop-2-en-1-one)-5-methyl phenyl] methanes and their dibromo derivatives have not yet been studied. It was, therefore, thought of interest to synthesize the title compounds from reported method[9] and to study their antimicrobial activity. The structure of these compounds has been established on the basis of elemental data and spectral analysis (IR, UV, NMR and mass).

EXPERIMENTAL

All melting points were taken in silicon oil bath instrument in open capillary and are uncorrected. Purity of the compounds was checked by TLC on silica gel-G. IR-spectra were recorded on Perkin-Elmer spectrophotometer, PMR spectra on Bucker AC 300 F NMR spectrophotometer at 300 MHz, mass spectra on Jeol D-300 (EI/CI) and UV-spectra on Shimadzu UV-160 spectrophotometer.

Preparation of 1,1-bis-[2-hydroxy-3-(3-aryl-prop-2-en-1-one)-5-methyl pheny] methane (4a–f)

Bis-ketone (0.01 mole) was condensed with aromatic aldehydes (0.02 mole) in presence of 40% alkali (8 mL) in alcoholic medium. The reaction mixture was kept overnight. Then it was decomposed by 1 : 1 HCl. The product obtained was

filtered, washed with 2% sodium bicarbonate and water and crystallised from acetic acid.

Spectral Interpretation of (4a)

IR (ν_{max}) cm^{-1}: 2834 ν(methyl) Ar—C—H Str., 1632 ν(C=O), 1454 ν(C=C), 1259 ν(C—O); ^1H NMR (δ): 2.1 (s, 6H, two $—CH_3$), 3.5 (s, 2H, —OH), 3.8 (s, 2H, CH_2), 4.5 (d, 1H, CH_A), 5.1 (d, 1H, CH_B), 6.4–7.6 (m, 14H, Ar—H); mass (m/z): 488 (M+); UV(λ_{max}): 340 nm, ($n \rightarrow \pi^*$).

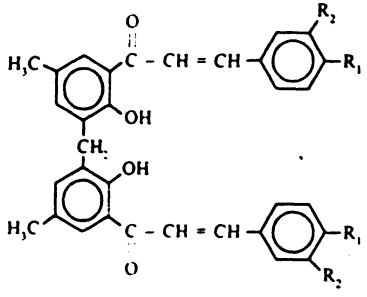
Preparation of 1,1-bis-[2-hydroxy-3-(2,3-dibromo-3-aryl-propan-1-one)-5-methyl phenyl] methane (5a–f)

To the solution of bis-chalcone **(4a–f)** (0.01 mole) and acetic acid (10 mL), bromine in acetic acid was slowly added with constant stirring. The reaction mixture was kept for 1 h at room temperature. The product obtained was filtered, washed and dried and crystallized from acetic acid.

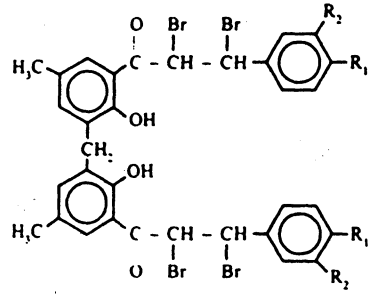
Spectral Interpretation of (5a)

IR (ν_{max}) cm^{-1}: 2923 ν(C—H str.), 1634 ν(C=O), 1451 ν(C=C), 1262 ν(C—O): ^1H NMR (δ): 2.1 (s, 6H, two $—CH_3$), 3.4 (s, 2H, CH_2), 3.7 (s, 2H, —OH), 4.1 (d, 1H, CH_A), 5.2 (d, 1H, CH_B), 6.8–7.6 (m, 14H, Ar—H); UV (λ_{max}): 347 nm, ($n \rightarrow \pi^*$).

Antimicrobial Activity: The titled compounds were screened for their antimicrobial activities using different microorganisms like *E. Coli, S. aureus, Pr. vulgaris, E. areogenes, Ps. aeruginosa, S. typhi, Pr. mirabilis*, by using paper disc method[10] at a concentration 25 μg/mL in DMF as a solvent. After 24 h of inhibition at 37°C the zones of inhibition were measured in mm. These values were recorded in Tables 1 and 2.



(4a-f)



(5a-f)

System	a	b	c	d	e	f
R_1	-H	$-OCH_3$	-OH	$-NO_2$	-H	$-NH_2$
R_2	-H	-H	$-OCH_3$	-H	$-OCH_3$	-H

RESULTS AND DISCUSSION

From Table-1, it was observed that all the compounds **(4a–f)** showed activity against *E. coli*. Compounds **(4a)**, **(4d)** and **(4f)** were found strongly active while compounds **(4b)**, **(4c)** and **(4e)** showed moderate activity against *E. coli*. The compounds **(4a)** and **(4f)** showed moderate activity, compounds **(4b)**, **(4e)** showed weak activity and compounds **(4c)** and **(4d)** were found inactive towards *S. aureus*.

The compounds **(4a)**, **(4c)** and **(4e)** were found moderately active, compounds **(4b)** and **(4f)** showed weak activity and compound **(4d)** was found inactive towards *Pr. mirabilis*. The compounds **(4c)** and **(4d)** showed moderate activity against *Ps. aeruginosa* while compounds **(4b)** and **(4f)** showed weak activity and compounds **(4a)** and **(4e)** were found inactive towards the same.

TABLE-1
ANTIMICROBIAL ACTIVITIES OF 1,1-BIS-[2-HYDROXY-3-(3-ARYL-PROP-2-EN-1-ONE)-5-METHYL PHENYL] METHANES **(4a–f)**

Organism	4a	4b	4c	4d	4e	4f
S. aureus	+++	++	−−	−−	++	+++
E. coli	++++	+++	+++	++++	+++	++++
Pr. mirabilis	+++	++	+++	−−	+++	++
Ps. aeruginosa	−−	++	+++	+++	−−	++
E. aerogenes	−−	++++	+++	+++	−−	+++
S. typhi	−−	+++	+++	+++	−−	+++
Pr. vulgaris	−−	+++	++	+++	−−	−−

The compound **(4b)** showed strong activity, compounds **(4c)**, **(4d)**, **(4f)** were found moderately active and compounds **(4a)** and **(4e)** were found inactive against *E. aerogenes*. The compounds **(4b)**, **(4c)**, **(4d)** and **(4f)** showed moderate activity towards *S. typhi* and compounds **(4a)** and **(4e)** were found inactive towards the same micro-organism.

The compounds **(4b)**, **(4d)** showed moderate activity and compounds **(4a)**, **(4e)** and **(4f)** were found inactive against *Pr. vulgaris*.

From Table-2, it is clear that the compounds **(5a)**, **(5b)**, **(5e)** showed strong activity and compounds **(5c)**, **(5d)** and **(5f)** showed moderate activity towards *E. coli*. The compounds **(5a)**, **(5b)**, **(5c)** and **(5f)** showed moderate activity towards *S. aureus*. The compound **(5e)** showed weak activtiy and **(5d)** was inactive towards the same micro-organism. The compounds **(5b)** and **(5c)** showed moderate activity towards *Pr. mirabilis* and other compounds were found inactive towards the same. The compounds **(5a)**, **(5b)** and **(5c)** were moderately active, **(5f)** was weakly active and **(5d)**, **(5e)** were inactive towards *Ps. aeruginosa*.

Almost all the compounds were inactive toward *E. aerogenes* except compound **(5a)** which showed moderate activity. Almost all the compounds showed moderate activity towards *S. typhi*, while compounds **(5a)**, **(5c)** showed strong

activity; compounds **(5d)**, **(5f)** were moderately active and compounds **(5b)**, **(5e)** were found weakly active towards *Pr. vulgaris.*

TABLE-2
ANTIMICROBIAL ACTIVITIES OF 1,1-BIS-{2-HYDROXY-3-[2,3-DIBROMO-3-ARYL-PROPAN-1-ONE]-5-METHYL PHENYL} METHANES **(5a–f)**

Organism	5a	5b	5c	5d	5e	5f
S. aureus	+++	+++	+++	--	++	+++
E. coli	++++	++++	+++	+++	++++	+++
Pr. mirabilis	--	+++	+++	--	--	--
Ps. aeruginosa	+++	+++	+++	--	--	++
E. aerogenes	+++	--	--	--	--	--
S. typhi	+++	+++	+++	+++	++	+++
Pr. vulgaris	++++	++	++++	+++	++	+++

N.B: ++++ Strongly active, range > 12 mm; ++ Weakly active, range < 8 mm;
+++; Moderately active, range 8–12 mm; -- Inactive

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